AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of the claims in the application:

Listing of Claims:

1-44. (canceled)

45. (currently amended) A method of evaluating a compound for the ability to inhibit binding of an intracellular receptor region of an α-subunit of a voltage-gated ion channel to an amino-terminal inactivation region of an ion channel protein, wherein the ion channel protein is a potassium channel protein selected from the group consisting of Kvß1, Kvß1.2, Kvß1.3, Kvß3, Kv1.4, and Kv3.4, comprising:

a) providing a first peptide comprising an S4-S5 cytoplasmic loop of a ~~selected from the group consisting of an isolated~~ potassium channel alpha-subunit, ~~an isolated intracellular receptor region, and~~ or a biologically active fragment of said S4-S5 cytoplasmic loop ~~alpha-subunit~~;

b) providing a second peptide comprising an ~~selected from the group consisting of an isolated beta-cytoplasmic ion channel protein, an isolated~~ amino-terminal inactivation region of a potassium ion channel alpha- or beta-subunit, ~~and~~ or a biologically active fragment of said amino-terminal inactivation region ~~cytoplasmic protein~~;

c) contacting said first peptide and said second peptide with said compound; and

d) determining the ability of said compound to interfere with the binding of said first peptide with said second peptide, wherein a decrease in said binding in the presence of said compound compared to said binding in the absence of said compound indicates that said compound inhibits binding of said S4-S5 cytoplasmic loop ~~intracellular receptor region~~ to said amino-terminal inactivation region.

46. (currently amended) The method of claim 45, wherein said S4-S5 cytoplasmic loop is an S4-S5 cytoplasmic loop of ~~the voltage-gated channel protein~~ is a potassium channel protein selected from the group consisting of Kv1.1, Kv1.2, Kv1.3 Kv1.4, Kv1.5, Kv1.6, and Kv3.4.

47-49. (canceled)

50. (currently amended) A method for identifying compounds which inhibit N-type inactivation of a voltage-gated ion channel, comprising:

a) administering a compound to a modified host cell comprising:

i) a first hybrid protein comprising a DNA-binding domain of a transcriptional activator in polypeptide linkage to either 1) an S4-S5 cytoplasmic loop ~~intracellular receptor region~~ of an α-subunit of a voltage-gated ion channel; or 2) an amino-terminal inactivation region of an ion channel protein;

ii) a second hybrid protein comprising an activation domain of a transcriptional activator in polypeptide linkage to said S4-S5 cytoplasmic loop ~~intracellular receptor region~~ if said DNA-binding domain is in polypeptide linkage to said amino-terminal inactivation region or to said amino-terminal inactivation region if said DNA-binding domain is in polypeptide linkage to said S4-S5 cytoplasmic loop ~~intracecullular receptor region~~; and

iii) a reporter gene whose transcription is dependent upon the first hybrid protein and the second hybrid protein being bound to each other, thereby reconstituting a transcriptional activator;

b) incubating the modified host cell for a suitable period;

c) determining whether the administration of the compound inhibits expression of the reporter gene; and

d) identifying a compound which inhibits expression of the reporter gene as an inhibitor of N-type inactivation of said voltage-gated ion channel.

51. (canceled)

52. (new) A method for identifying an agent capable of modulating inactivation of an ion channel, said method comprising detecting binding of a first protein to a second protein in the presence or absence of a molecule of interest, wherein said first protein comprises an S4-S5 cytoplasmic loop of a voltage-gated ion channel, and said second protein comprises an amino-terminal inactivation region of an ion channel subunit, and wherein said first protein binds to said second protein in the absence of said molecule of interest, and a decrease in said binding in the presence of said molecule of interest as compared to that in the absence of said

molecule of interest is indicative that said molecule of interest is capable of modulating inactivation of said voltage-gated ion channel.

53. (new) The method of claim 52, wherein said S4-S5 cytoplasmic loop is an S4-S5 cytoplasmic loop of a potassium channel α-subunit, and said amino-terminal inactivation region is an amino-terminal inactivation region of a potassium channel α- or β-subunit.

54. (new) The method of claim 53, wherein said first protein further comprises a DNA-binding or transcription activation domain of a transcriptional activator, and said second protein further comprises:

a DNA-binding domain if said first protein comprises the transcription activation domain of said transcriptional activator, or

a transcription activation domain if said first protein comprises the DNA-binding domain of said transcriptional activator,

wherein binding of said first protein to said second protein forms a transcriptional activator.

55. (new) The method of claim 54, comprising expressing said first protein and said second protein in a host cell in the presence or absence of said molecule of interest, wherein binding of said first protein to said second protein activates expression of a reporter gene in said host cell.

56. (new) The method of claim 55, wherein said host cell is yeast.

57. (new) The method of claim 55, wherein said S4-S5 cytoplasmic loop is an S4-S5 cytoplasmic loop of a potassium channel α-subunit selected from the group consisting of Kv1.1, Kv1.2, Kv1.3, Kv1.4, Kv1.5, Kv1.6 and Kv3.4, and said amino-terminal inactivation region is an amino-terminal inactivation region of a potassium channel α- or β-subunit selected from the group consisting of Kvβ1, Kvβ1.2, Kvβ1.3, Kvβ3, Kv3.4, and Kv1.4.

58. (new) The method of claim 55, wherein said S4-S5 cytoplasmic loop is an S4-S5 cytoplasmic loop of potassium channel Kv1.1 or Kv1.4, and said amino-terminal inactivation region is an amino-terminal inactivation region of potassium channel Kvβ1.

59. (new) The method of claim 55, wherein said first protein consists essentially of said S4-S5 cytoplasmic loop and the DNA-binding or transcription activation domain of said transcriptional activator.

60. (new) The method of claim 55, wherein said S4-S5 cytoplasmic loop comprises SEQ ID NO:1 or SEQ ID NO:2, and said amino-terminal inactivation region comprises SEQ ID NO:5 or SEQ ID NO:6.

61. (new) The method of claim 53, wherein said first protein further comprises a first polypeptide selected from a peptide binding pair, and said second protein further comprises a second polypeptide selected from said peptide binding pair, and wherein binding of the first polypeptide to the second polypeptide in a host cell is capable of producing a detectable event or a selectable phenotype in said cell.

62. (new) The method of claim 61, wherein said cell is yeast.

63. (new) The method of claim 61, wherein said S4-S5 cytoplasmic loop is an S4-S5 cytoplasmic loop of a potassium channel α-subunit selected from the group consisting of Kv1.1, Kv1.2, Kv1.3, Kv1.4, Kv1.5, Kv1.6 and Kv3.4, and said amino-terminal inactivation region is an amino-terminal inactivation region of a potassium channel α- or β-subunit selected from the group consisting of Kvβ1, Kvβ1.2, Kvβ1.3, Kvβ3, Kv3.4, and Kv1.4.

64. (new) The method of claim 61, wherein said S4-S5 cytoplasmic loop is an S4-S5 cytoplasmic loop of potassium channel Kv1.1 or Kv1.4, and said amino-terminal inactivation region is an amino-terminal inactivation region of potassium channel Kvβ1.

65. (new) The method of claim 53, wherein one protein selected from said first and second proteins further comprises a cell compartment localization domain capable of recruiting said one protein to a cell compartment of a host cell, and the other protein selected from said first and second proteins comprises an effector protein, and wherein recruitment of said one protein to the cell compartment and binding of said first protein to said second protein produce a detectable event or a selectable phenotype in said host cell.

66. (new) An agent identified according to claim 52, wherein said agent inhibits binding between said S4-S5 cytoplasmic loop and said amino-terminal inactivation region.

67. (new) A method for identifying an agent capable of modulating an interaction between an S4-S5 cytoplasmic loop of a potassium channel α-subunit and an amino-terminal inactivation region of a potassium channel α- or β-subunit, said method comprising:

expressing a first protein and a second protein in a host cell, wherein said first protein comprises (1) said S4-S5 cytoplasmic loop and (2) a DNA-binding or transcription activation domain of a transcriptional activator, wherein said second protein comprises (1) said amino-terminal inactivation region and (2) a DNA-binding domain if said first protein comprises the transcription activation domain of said transcriptional activator or a transcription activation domain if said first protein comprises the DNA-binding domain of said transcriptional activator, and wherein said S4-S5 cytoplasmic loop is capable of binding to said amino-terminal inactivation region in the absence of a molecule of interest, and binding of said first protein to said second protein forms a transcriptional activator capable of activating expression of a reporter gene in said host cell;

contacting the molecule of interest with said host cell; and

detecting any change in said expression of the reporter gene,

wherein a decrease in said expression is suggestive that the molecule of interest is capable of modulating the interaction between said S4-S5 cytoplasmic region and said amino-terminal inactivation region.

68. (new) A method for identifying an agent capable of modulating an interaction between an S4-S5 cytoplasmic loop of a potassium channel α-subunit and an amino-terminal inactivation region of a potassium channel α- or β-subunit, said method comprising:

expressing a first protein and a second protein in a host cell, wherein said first protein comprises said S4-S5 cytoplasmic loop and a first polypeptide, and said second protein comprises said amino-terminal inactivation region and a second polypeptide, and wherein said S4-S5 cytoplasmic loop binds to said amino-terminal inactivation region in the absence of a molecule of interest, and interaction or close proximity between said first polypeptide and said second polypeptide is capable of producing a detectable event or a selectable phenotype in said host cell;

contacting the molecule of interest with said host cell; and

detecting any change in said detectable event or selectable phenotype,

wherein a change in said event or phenotype is suggestive that the molecule of interest is capable of modulating the interaction between said S4-S5 cytoplasmic region and said amino-terminal inactivation region.